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CLINICAL APPLICATION OF FAT EMULSIONS

by

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I. INTRODUCTION

We have carried on our fundamental studies on the parenteral nutritional supplement of fat for the past several years and have succeeded in developing a 20% sesame oil emulsion which fulfills this aim. We have also been able to clarify for the most part the process of metabolism of the fat injected intravenously. The purpose of this study was to find out whether the same effect could be obtained by intravenous administration of this preparation in man as was obtained in the experimental animals.

II. REINVESTIGATION OF THE EMULSION

Before applying this sesame oil emulsion clinically, the following points should of course be re-examined closely.

- (a) The danger of incurring a tissue reaction
- (b) The danger of forming fat emboli
- (c) The danger of hemolysis
- (d) The danger of incurring fatty liver
- (e) Prevention of colloid-shock

To clarify problems (a) and (b) electro-encephalographic studies were conducted. It was found that with the fat emulsions prepared from fats containing a relatively high percentage of triglycerides of lower fatty acids there appeared marked spikes and slow waves, while with the emulsions prepared from the sesame oil containing only the triglycerides of the higher fatty acids these were not observed. It is clear from these findings, that there is no danger of tissue irritation or fat embolism even if the sesame oil emulsion is applied to man. This was verified by examining the plasma cells in the omentum which was taken out after the repeated, long-term administration.

Problem (c) was studied by examining hemosiderin deposition histologically in the spleen. It was found that the hemolysis also occurred with the sesame oil emulsion containing only the triglycerides of higher fatty acids, though the hemolysis was far less than that seen with the preparation containing a high percentage of triglycerides of lower fatty acids. With further modification of the preparation, the 20% sesame oil emulsion which is free of this danger was devised.

In regards to (d), we have found that repeated long-term intravenous administration of the fat emulsions containing a large quantity of triglycerides of lower

fatty acids results in a heavy deposition of phospholipid in the liver parenchymal cells which finally evolves into a fatty liver, but this does not occur in the case of the sesame oil emulsion administered in the same manner.

It can be seen from these results that the use of the sesame oil which contains only the triglycerides of higher fatty acids is rational. It has been stated that the intravenous injection of a concentrated colloid solution results in a physiological colloid shock. When the 20% sesame oil emulsion which is a kind of colloid suspension is injected intravenously without modification, this reaction will take place and the so-called tachyphylaxis manifestations, such as flushing of face and oppression of the chest, will become apparent. Measures to combat with this must therefore be taken. The most logical method would be to raise the level of fat in the blood gradually in the same manner as fat is absorbed when taken by mouth. This is simple to say but difficult to actually carry out. According to the study by Prof. Masaki on colloid shock in which it was shown that the phenomenon occurs only after the first injection of the colloid solution, the method described in the next section was devised and it has become possible to prevent the troublesome reactions caused by colloid shock. It can therefore be said that the 20% sesame oil emulsion most recently prepared is free from the various dangers and may be safely given intravenously to man.

III. METHOD OF ADMINISTRATION

From the standpoint of controlling colloid shock, the following method must be taken for the initial injection. The initial dose shall be 4~5 cc of the 20% sesame oil emulsion diluted about 10-fold with 5~20% glucose solution and shall be injected intravenously at a very slow rate. After 5~10 minutes, a mixture of 50cc of 20% sesame oil emulsion, 40 cc of 20% glucose solution and various vitamins (usually 10 mg. thiamine, 10 mg. riboflavin, 100 mg. *l*-ascorbic acid and when required nicotinamide and pantothenic acid) shall be injected intravenously. This special method need not be followed in the succeeding injections and a mixture of 50 cc of 20% sesame oil suspension, 40 cc of 20% glucose solution and various vitamins may be injected directly. There is no need to wait for several days between injections and the injection may be given 2 times a day, morning and evening, without fear of troublesome reactions and it is possible to administer the daily requirement of fat, 20 g, parenterally. When more than 1 day has elapsed between injections, it is best to follow the initial method of injection in order to prevent colloid shock.

In administering fat parenterally, 20% glucose solution has been given concomitantly as a rule. This was based on the finding in the preliminary studies that glucose is required for the smooth metabolism of fat administered parenterally.

IV. NUTRITIONAL EFFECT OF FAT ADMINISTERED PARENTERALLY

The following 2 experiments were conducted in order to see if the intravenous injection of this preparation in man would have the same effect on economization

of protein and stored fat as was observed in the experimental animals.

(a) *Administration in very poorly nourished patient*

As space is limited, one representative case is presented here. The patient had swallowed strong alkali in order to commit suicide and, though prompt measures had prevented death, a marked stenosis of the esophagus had resulted with complete inability to take food by mouth.

A jejunal fistula had been constructed surgically and forced feeding from this opening had been attempted, but there had been no improvement in the nutritional state. One month after the construction of the fistula, intravenous administration of 20g fat daily was started. The nitrogen balance which had been on the negative side became normal from about one week after starting the injections and the urinary creatinine gradually decreased. The quantity of circulation serum returned to normal levels, and, as the results, the serum protein level which had become abnormally high due to dehydration gradually dropped. The total protein content of the circulating blood increased and there was a marked increase in body weight. There was an improvement in the serum electrophoretic pattern, a raise in A/G ratio, an improvement of liver function and other signs of a marked nutritional improvement (Fig. 1, 2 and 3).

Abnormal increases in β - and γ -globulin which would indicate accumulation of the injected fat in the blood were not observed even after 1 month of continuous daily administration. Signs of sclerotic changes in the coronary arteries were not observed by electrocardiograms.

Fig. 1. Effect of Sesame Oil Emulsion Injection on Nitrogen Balance in a Case of Esophageal Stenosis (Alkali Swallowing).

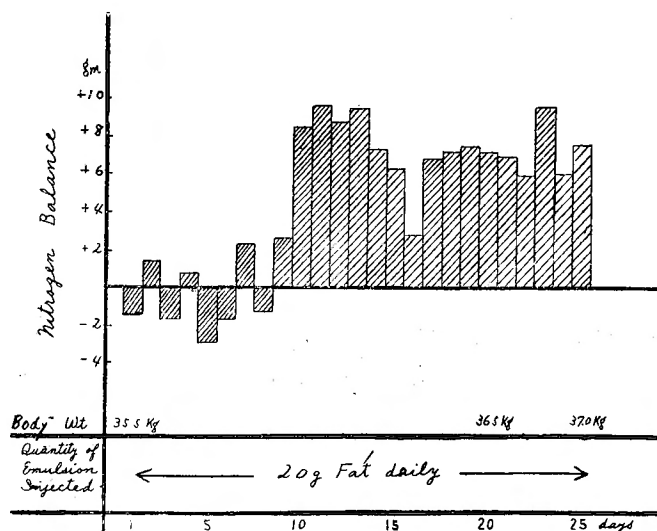
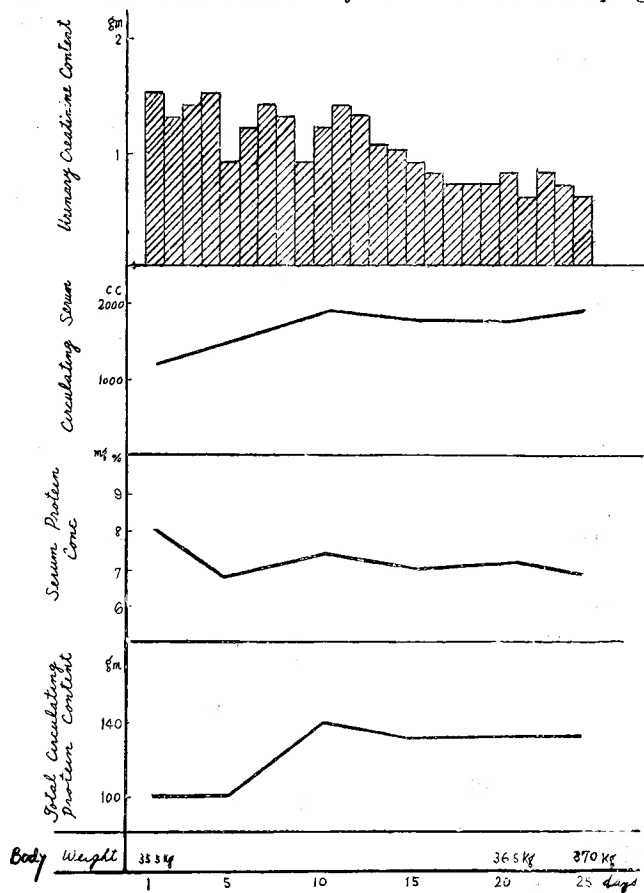
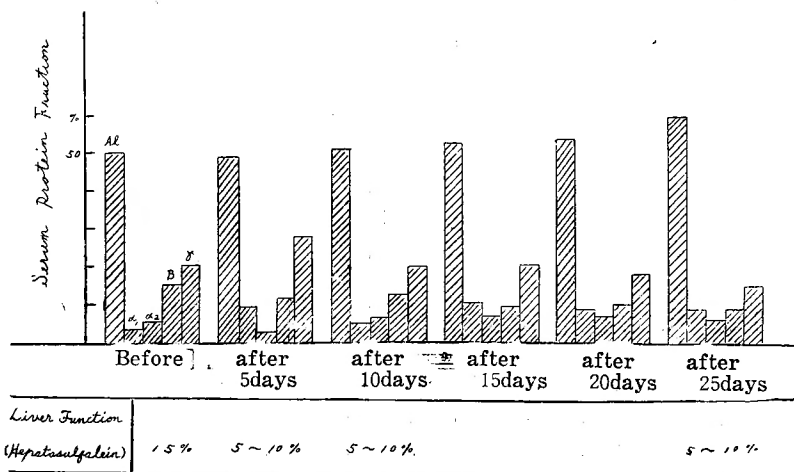
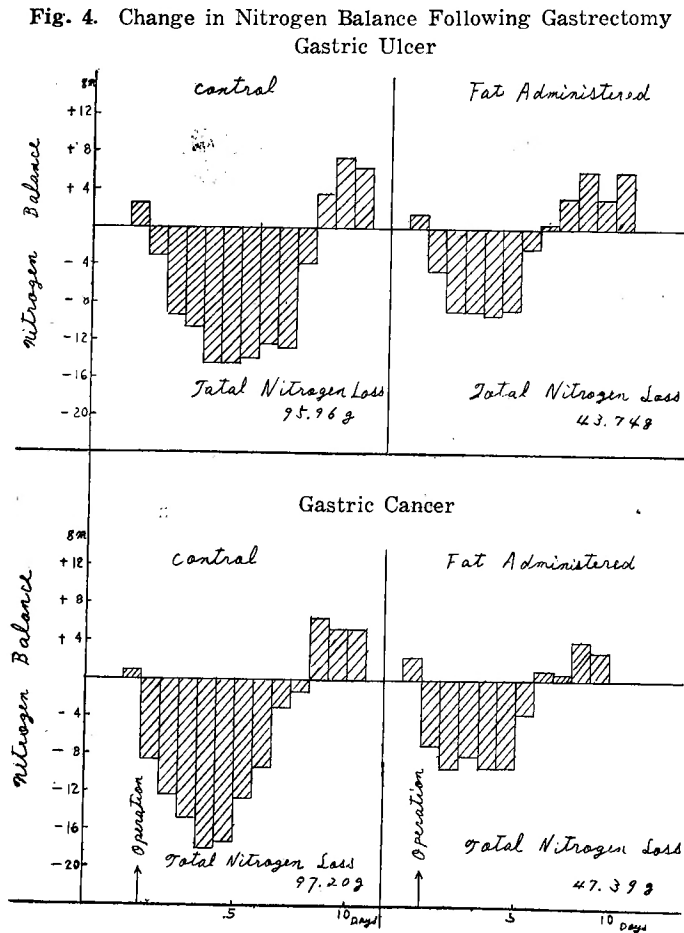


Fig. 2. Effect of Sesame Oil Emulsion Injection in a Case of Esophageal Stenosis**Fig. 3** Effect of Sesame Oil Emulsion Injection on the Serum Protein Fraction

(b) Administration prior to and after surgical operation.

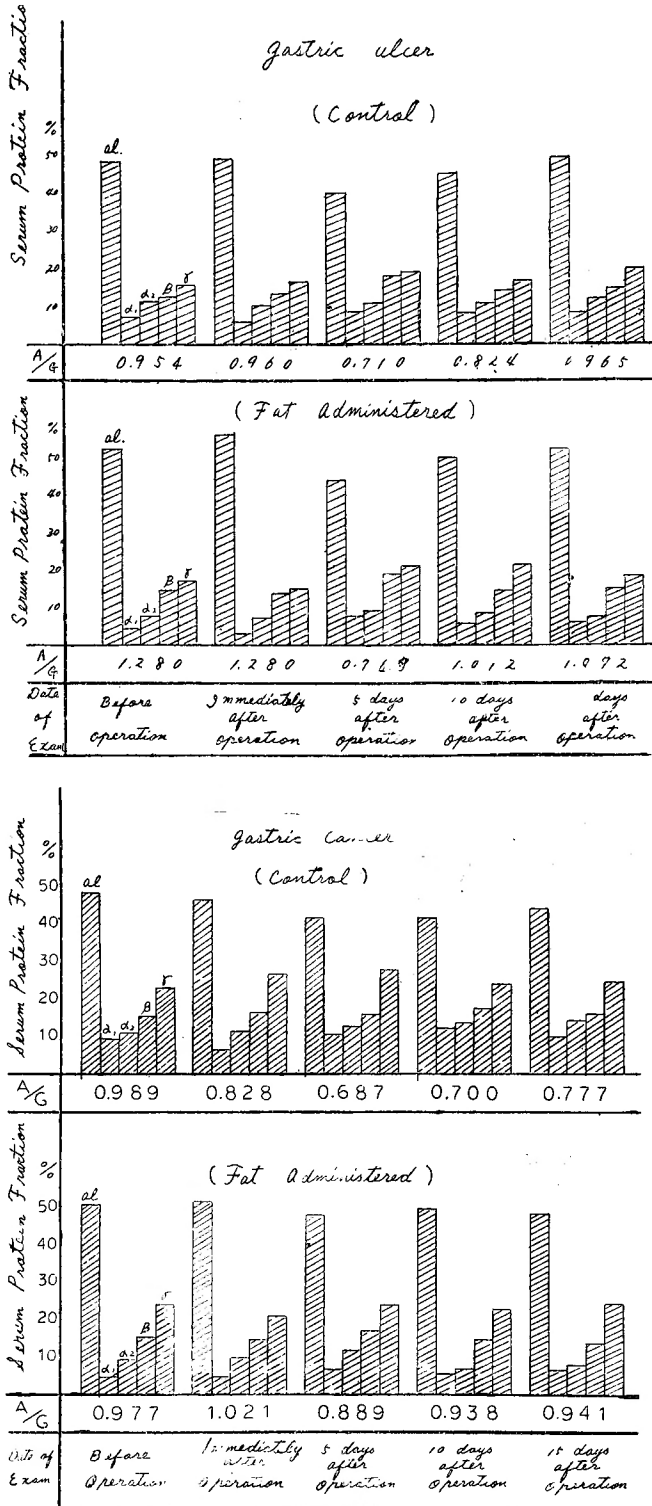
The fat emulsion preparation was administered for 5 days before and for 10 days after surgical operation, and the nutritional effect was examined. Twenty grams of it was administered every day intravenously. Cases of gastric cancer and gastric ulcer in which gastrectomy had been successfully performed were selected for the study.

In the gastric cancer control and the gastric ulcer control, there was a nitrogen loss of 97.20 g and 95.96 g respectively after gastrectomy. In the group given fat parenterally, the nitrogen loss was only 47.39 g and 43.74 g respectively and there was a marked economization of protein. It was also found that the period of negative nitrogen balance following surgical operation was markedly shortened in the fat administered group and there was an early change to the state of catabolism (Fig. 4).



The examination of the electrophoretic pattern showed that in the fat injected group, the return to a normal pattern took place within 10 days after surgical operation in both the gastric cancer case and the gastric ulcer case, while in the

Fig. 5. Serum Electrophoretic Pattern before and after Gastrectomy



controls a normal pattern was not observed even after 15 days in the gastric cancer case and the pattern became normal after 15 days in the gastric ulcer case. Furthermore, there was no abnormal raise in β - and γ -globulin with repeated injections after surgical operation showing that the injected fat was smoothly utilized and had a strong economizing action on protein. It is suggested that postoperative recovery was markedly accelerated by the parenteral administration of fat (Fig. 5 and Table 1). The above are the observations from the viewpoint of protein metabolism alone, but even from these results it is clear that this preparation is effective.

Table 1 Rate of Loss in Body Weight (gastric cancer)

	5 days after Operation	10 days after Operation	15 days after Operation
Control	-6.7%	-5.3%	-5.7%
Fat Administered	-5.4%	-2.6%	-2.9%

V. CONCLUSION

The clinical application of the 20% sesame oil emulsion is extremely effective from a nutritional standpoint and there is no danger of any troublesome reaction, so that parenteral nourishing of fat can be carried out safely together with the parenteral supplement of amino acids, glucose, vitamins and electrolytes. At present, 20 grams fat is being supplemented parenterally but the question of the optimum dosage must be studied further.

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